REMARKS

This response supplements the RCE and Response filed by Applicants on May 31, 2011. Arguments and Amendments made in the previous response are not repeated here. Claim amendments presented here are made assuming entry of the previous claim amendments filed May 31, 2011. Arguments made in the previous response also apply to the presently amended claims. Applicants request the Examiner to kindly consider the Inventors' Declaration attached hereto, the claim amendments and remarks and request favorable action thereon.

I. Status of Claims

Claims 1-25 and 34-36 were pending at the time of the Final Office Action (herein after FOA). Claims 1-4, 13, 15, 18, 19, 21-24 and 34-36 were amended without prejudice or disclaimer in the Response and RCE filed by Applicants on May 31, 2011. Applicants now present, further amendments to claims 1, 15 and a new claim 37. Accordingly, claims 1-25 and 34-37 are now pending in the application.

Applicants reserve the right to prosecute any amended or deleted matter in one or more continuation applications. No new matter has been added by the claim amendments. Support for amendments to claim1 may be found in the originally-filed specification at least on page 30, lines 9-16; paragraph adjoining pages 32-33, page 13, lines, 30-37 (which describe analysis of isolated nucleic or protein components, thereby showing that proteins and/or nucleic acids isolated by the claimed method are substantially intact); paragraph abridging pages 20 and 21; page 21, lines 13-35; page 25, lines 30-37; and page 26, lines 3-10 which specifically states "one of the main advantages of the method of the invention is that one or more off DNA, RNA and protein can be isolated from the same sample ready for analysis." Support for amended claim 15 may be found at least on page 30, lines 13-16. Support for new claim 37 may be found in the specification at least at page 30, lines 9-16, paragraph adjoining pages 32-33 and page 46 in its entirety and page 47, lines 1-22.

Additional Arguments for the Rejections under 35 USC § 103(a)

A. Claims 1-25 and 34-36 stand rejected as allegedly being unpatentable over U.S. Patent No. 6,255,477 to Kleiber et al. ("Kleiber") in view of U.S. 6,723,510 to Lubenow ("Lubenow") and further in view of Schubler et al. (TIG, 1995, 11, 378-379) ("Schubler").

Applicants respectfully traverse this rejection. In addition to the amendments previously presented on May 31, 2011, Applicants now present further amendments to claim 1. Claim 1 now recites additional limitations of "contacting said sample with a first magnetic particulate solid support under conditions wherein nucleic acid components bind to the first magnetic particulate solid supports in a sequence independent manner and the protein components remain substantially intact;" and "contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, under conditions wherein protein components contained in the sample bind to the second magnetic particulate solid support through a chromatographic interaction and the nucleic acid components remain substantially intact;" and "thereby isolating nucleic acid components and protein components that are substantially intact." (marked up version of amended claim 1)

Differences over Kleiber:

As was already acknowledged by the Examiner, on page 8 of the FOA, "Kleiber does not teach explicitly the binding proteins to the second magnetic particulate solid supports by effecting a chromatographic interactions and separating the plurality of first magnetic particulate supports and the second magnetic particulate supports bound to the proteins from unbound components in the sample."

Applicants respectfully submit that Kleiber fails to teach that it is even possible to isolate "protein components that are substantially intact," as recited by present claim 1, since the methods of Kleiber describe the use of "chaotropes" which as is known to one of skill in the art denatures proteins. See Kleiber in at least FIG. 1; and column 6, lines 22-29; column 8, lines 33-36.

For example, column 6, lines 22-29 of Kleiber state:

> be bound. The procedure for binding native nucleic acids to glass particles can be analogous to the procedure described in the prior art. It is preferably performed in the presence of chaotropic salts with a concentration of between 2 and 8 mol/l, and preferably between 4 and 6 mol/l. Chaotropic salts can be sodium iodite, sodium perchlorate, guanidinium thiocyanate, guanidinium isothiocyanate or guanidinium hydrochlorite. Other compounds are also possible.

For example, column 8, lines 33-36 of Kleiber state;

> nor destroyed. The cells are then destroyed, i.e., lysed. This can be performed, for instance, by treating the cells with chaotropic salts. Other possibilities include the application of proteinases and detergents.

In stark contrast to the teachings of Kleiber, the present specification, on page 30, lines 9-16, states:

> The only requirement is that an appropriate method is chosen such that the species of nucleic acid and protein to be analysed in the subsequent procedure remain substantially intact, i.e. substantially non-degraded.
> The use of agents such as solvents, alcohols and chaotropes in isolation methods is sometimes disadvantageous. The present invention affords the advantage that the use of such agents may be avoided. Thus, whilst lysis methods such as those mentioned above using such agents may be employed, in advantageous embodiments of the invention the use of such agents is avoided. "
> (emphasis added)

Thus, Kleiber in fact "teachs away" from the "protein isolation" embodiments of claim 1 which recite "thereby isolating….protein components that are substantially intact." This point is also noted and elaborated in the Inventor Declaration of inventor Marie Bosnes, in sections that describe Kleiber's use of chaotropes and proteinases, which are agents to be avoided according to the present application.

Differences over Lubenow:

In view of the above, Kleiber may not be combined with Lubenow, since it teaches away from the possibility of "isolating protein components that are substantially intact." In addition, Lubenow also fails to teach or suggest any missing links that are not taught by Klieber. As discussed by Applicants in the response filed May 31, 2011, Lubenow fails to teach or suggest the separation of both nucleic acids and proteins from a single sample using magnetic particles for each process in a single method. At best Lubenow appears to describe isolating a biomolecule using a specific-affinity tag such as isolating a fusion protein having a His-tag by an affinity magnetic bead matrix (immobilized metal ion affinity chromatography (IMAC)) and mentions oligo dT magnetic particles for binding polyA RNA. However, there is no teaching or suggestion of how the skilled artisan may practically combine the two isolations into one method and there is further no teaching or suggestion of conditions that would allow both processes to be conducted for one sample with each component (nucleic acid and protein remaining intact) as in the present claims.

Furthermore, Lubenow utterly fails to teach or suggest at least the following elements of currently amended claim 1 including "contacting said sample with a first magnetic particulate solid support under conditions wherein nucleic acid components bind to the first magnetic particulate solid supports in a sequence independent manner and the protein components remain substantially intact;" and "contacting the sample with a second magnetic particulate solid support distinct from the first magnetic particulate solid support, under conditions wherein protein components contained in the sample bind to the second magnetic particulate solid support through a chromatographic interaction and the nucleic acid components remain substantially intact;" and "thereby isolating nucleic acid components and protein components that are substantially intact."

For example, as described in the Inventor Declaration of Inventor Marie Bosnes, who is a person of ordinary skill in the art, if the teachings of Kleiber and Lubenow were to be combined they would fail to achieve isolation of "nucleic acid components and protein components that are substantially intact," as recited by claim 1 and its dependents at least for the following reasons:

1) "the detergents described by Lubenow at column 4, lines 13-27, will not allow binding of nucleic acids to a glass surface as described by Kleiber;" (as recited in Inventor Declaration, section 4c)

2) as described earlier, the buffer of Kleiber, which has chaotropes, will denature proteins and will therefore not allow for isolation of "protein components that are substantially intact" as recited by claim 1; and

3) substituting ion-exchange beads for streptavidin beads or other specific-affinity beads would not work in a surrounding chemical solution containing high salt and chaotropes of Klieber. (as recited in Inventor Declaration, section 4b)

Differences over Schubler:

Applicants have already demonstrated that Schubler describes no more than poly A-RNA separation using oligo dT columns and that Schubler utterly fails to teach protein separation in the same sample using magnetic particles. This is further elaborated the Inventor Declaration of Marie Bosnes.

One of skill in the art, upon review of Klieber, alone or in combination with Lubenow and/or Schubler, would agree that, absent the teachings of the present specification, one of skill in the art would not arrive at the teachings of currently amended independent claim 1. Since all dependent claims incorporate by reference the limitations of their independent claims (see 35 U.S.C. §112, ¶4), claims 2-25 and 34-36 (and new claim 37) also incorporate by reference at least the elements recited above that are not taught by Klieber alone or in combination with Lubenow and/or Schubler. Accordingly, at least for analogous reasons, claims 2-25 and 34-37 are also free of the obviousness rejections.

In view of this additional evidence, Applicants respectfully request the withdrawal of rejections under 35 U.S.C. §103(a) and an allowance of claims 1-25 and 34-37.

CONCLUSION

Applicants believe that all outstanding matters in this case have been addresses. In view of the above amendment to claims and remarks, it is submitted that this application and pending claims are now in condition for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (512) 721-3657.

Respectfully Submitted,

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